

Figure 1 – PEPTIDES DERIVED FROM NATURAL CASEIN STIMULATE MURINE NATURAL KILLER (NK) CELL ACTIVITY.

| Group Ex. No | > | 1:25 | | 1:50 | |
|-----------------|---|---------|---------|---------|---------|
| | | Control | Chay-13 | Control | Chay-13 |
| 1 | | 16.10 | 43.80 | 27.50 | 62.80 |
| 2 | | 25.70 | 45.40 | 18.20 | 43.40 |
| 3 | | 0.00 | 3.10 | 0.00 | 35.00 |
| 4 | | - | - | 9.00 | 35.00 |
| Average | | 13.93 | 30.77 | 13.68 | 44.05 |
| SD | | 12.99 | 23.97 | 11.84 | 13.11 |

CHAY-13 EFFECT ON NK ACTIVITY

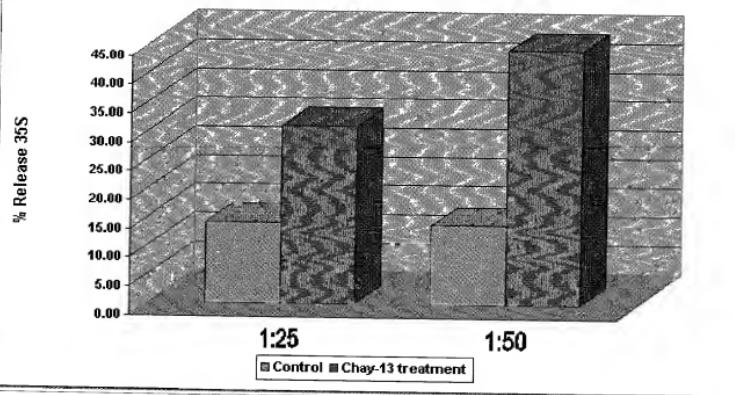


Figure 2a – EFFECT OF PEPTIDES DERIVED FROM NATURAL CASEIN ON HUMAN NATURAL KILLER (NK) CELL ACTIVITY IN CELLS FROM A SINGLE DONOR.

| Dose > | 0 | 5 | 10 | 25 | 50 | 100 | 250 | 500 |
|--------|-----|-----|------|------|------|------|------|------|
| 1:50 | 3.9 | 5.4 | 11.3 | 10.9 | 9.1 | 8.3 | 12.5 | 15.5 |
| 1:100 | 4.6 | 5.1 | 12.4 | 12.8 | 11.9 | 10.8 | 12.1 | 14.9 |

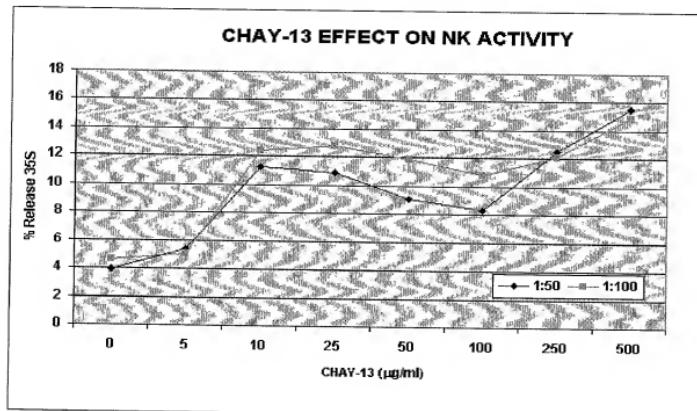


Figure 2b SELECTIVE STIMULATION OF HUMAN NATURAL KILLER (NK) CELL ACTIVITY BY PEPTIDES DERIVED FROM NATURAL CASEIN.

| Patient | Type | 0 | 10 | 25 | 100 | 250 | 500 |
|---------|---------|------|------|------|------|------|------|
| 1 | Normal | 13 | 15 | 15 | 12 | 13 | 15 |
| 2 | NHL | 10.1 | 13.8 | 14.3 | - | 15.8 | 13.7 |
| 3 | NHL | 3.5 | 10.4 | 8.4 | 10.8 | - | - |
| 4 | Br. Ca. | 4.2 | 2.7 | 7.1 | 7.7 | 5.9 | 10.1 |
| 5 | - | 12.2 | 18.1 | 19.1 | 14.3 | 13.4 | 15.8 |
| 6 | - | 17 | 15 | 15 | 15 | 13 | 9 |

Figure 3a – PEPTIDES DERIVED FROM NATURAL CASEIN STIMULATE PROLIFERATION OF HUMAN CD₅₆ SURFACE ANTIGEN POSITIVE (NK) CELLS.

| Patient | Control | Chay-13 |
|-------------|---------|---------|
| 1 | 0.60 | 0.20 |
| 2 | 0.60 | 1.90 |
| 3 | 0.10 | 0.90 |
| 4 | 0.40 | 3.30 |
| 5 | 1.50 | 3.70 |
| Mean | 0.64 | 2.00 |
| SD | 0.52 | 1.50 |

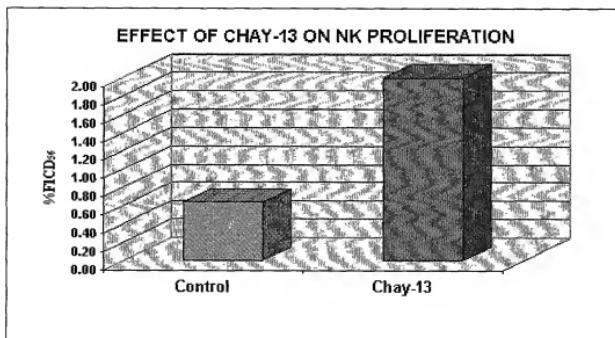


Figure 3b – PEPTIDES DERIVED FROM NATURAL CASEIN STIMULATE PROLIFERATION OF HUMAN CD₃ SURFACE ANTIGEN POSITIVE (T) CELLS.

| Patient | Control | Chay-13 |
|-------------|--------------|--------------|
| 1 | 7.90 | 10.40 |
| 2 | 8.19 | 10.46 |
| 3 | 12.82 | 58.64 |
| 4 | 62.86 | 50.44 |
| 5 | 5.49 | 47.76 |
| Mean | 19.45 | 35.54 |
| SD | 24.41 | 23.27 |

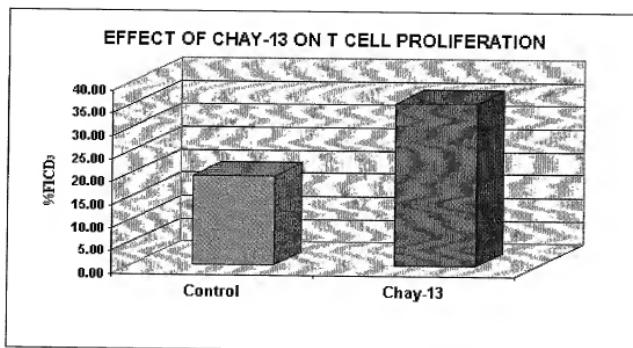


Figure 3c – PEPTIDES DERIVED FROM NATURAL CASEIN STIMULATE PROLIFERATION OF HUMAN CD₅₆ AND CD₃ SURFACE ANTIGEN POSITIVE (NK/T) CELLS.

| Patient | Control | Chay-13 |
|-------------|-------------|-------------|
| 1 | 8.00 | 25.00 |
| 2 | 1.1 | 4.3 |
| 3 | 0.1 | 0.85 |
| 4 | 2.77 | 3.89 |
| 5 | 1.74 | 4.34 |
| 6 | 0.84 | 4.53 |
| 7 | 0 | 2.55 |
| Mean | 2.08 | 6.49 |
| SD | 2.78 | 8.27 |

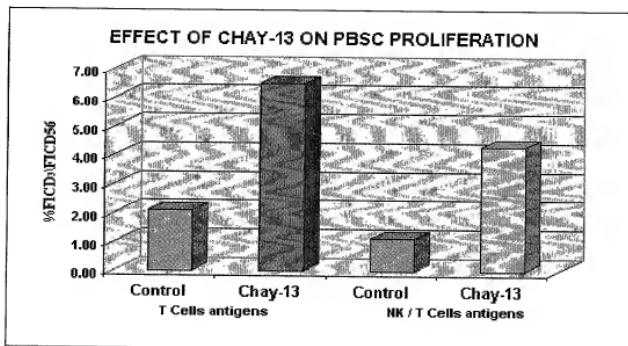




FIG. 4 - The effect of synthetic peptides on the stimulation of NK cells activity in cultured human PBC.

| PEPTIDE | 0 | 10 | 25 | 100 | 250 | 500 | ug/ml |
|---------|------|-------|------|------|------|------|--------------|
| 1a | 4.3% | *1880 | 7% | 1803 | 6.2% | 2006 | 9.2% |
| 2a | 4.3% | 1762 | 5.6% | 1908 | 7.1% | 1840 | 6.7% |
| 3a | 4.3% | 2003 | 9.1% | 1868 | 7.1% | 1847 | 6.8% |
| | | | | | | | 1768 5.6% 1a |
| | | | | | | | 1883 7.4% 2a |
| | | | | | | | 1997 9.1% 3a |

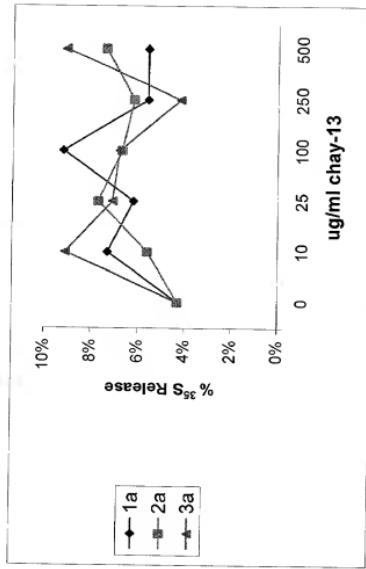


FIG. 5a-c – PEPTIDES DERIVED FROM NATURAL CASEIN STIMULATE PROLIFERATION OF CULTURED HUMAN PERIPHERAL BLOOD STEM CELLS.

| Blood origin | Incubation period (days) | Control | 50 ($\mu\text{g/ml}$) | 100 ($\mu\text{g/ml}$) | 300 ($\mu\text{g/ml}$) | 600 ($\mu\text{g/ml}$) |
|--------------|--------------------------|---------|-------------------------|--------------------------|--------------------------|--------------------------|
| PBSC | 20 | 1663 | 3007 | 1800 | 4306 | 3310 |
| PBSC | 15 | 741 | 1612 | 784 | - | 920 |
| BM normal | 21 | 675 | - | 660 | 834 | 817 |
| BM Auto | 21 | 945 | - | 916 | 1537 | 1284 |
| BM 1 | 21 | 1829 | 4217 | 4396 | 9178 | 1446 |
| BM 2 | 21 | 1829 | 5039 | 2939 | 1496 | - |
| CBI | 14 | 1159 | 1191 | 1694 | 3961 | 3297 |
| CB2 | 14 | 3434 | - | 10882 | - | 13560 |

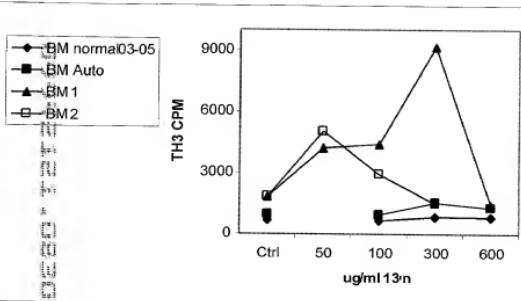


FIG. 5b

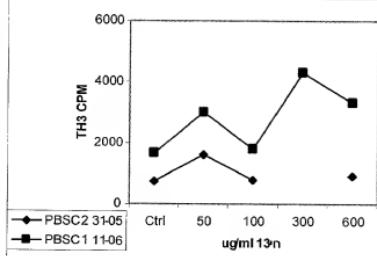


FIG. 5a

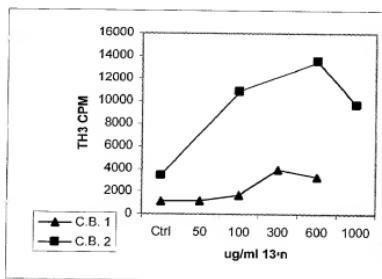


FIG. 5c

Figure 6

**PEPTIDES DERIVED FROM NATURAL CASEIN STIMULATE
PROLIFERATION OF NORMAL HUMAN HEMATOPOIETIC
CELLS.**

| Donor | Days Of Incubation | Factors Added | Relative Cell No. X 10 ⁴ /ml | | | | |
|----------------|-----------------------|-------------------------------|---|-----|-----|-----|-----|
| | | | 0 | 25 | 100 | 250 | 500 |
| Bone Marrow | 14 | EPO, hIL-3, hSCF, AB serum | 41 | 64 | - | 67 | 51 |
| Cord Blood | 13 | EPO, hIL-3, hSCF, AB serum | 27 | 158 | 66 | 50 | - |

Synthetic Casein-Derived Peptides

FIGURE 7

EFFECT OF PEPTIDE LENGTH ON RELATIVE CELL DISTRIBUTION (DIFFERENTIAL COUNT (%)

| Identification | PEPTIDE'S LENGTH | CONC. (μ g) | Mo ⁺ | RELATIVE CELL DISTRIBUTION (%) | | | | | | | | | | EOS/BAS | MITOSSES | TOTAL |
|--------------------------------------|------------------|------------------|-----------------|--------------------------------|----------|---------|----------|-----------|----------|-----------|--------------|-----------------|------|---------|----------|-------|
| | | | | PMN | EARLY MK | LATE MK | TOTAL MK | EARLY RBC | LATE RBC | TOTAL RBC | PLASMA CELLS | DENDRITIC CELLS | | | | |
| 74 | 2 | 25 | 17.8 | 2.6 | 3.5 | 3.7 | 7.2 | 15.8 | 20.4 | 36.2 | 8.3 | 23.0 | 2.8 | 4 | 544 | |
| 1P | 3 | 25 | 11.3 | 2.9 | 8.8 | 5.4 | 14.2 | 16.5 | 38.6 | 55.1 | 6.7 | 7.5 | 2.3 | 9 | 521 | |
| 2P | 4 | 25 | 6.1 | 2.3 | 7.4 | 9.1 | 16.5 | 19.4 | 51.8 | 71.2 | - | - | 0.6 | 4 | 700 | |
| 3P | 5 | 25 | 12.9 | 1.8 | 16.0 | 16.9 | 32.9 | 18.9 | 23.4 | 42.3 | 2.2 | 7.4 | 0.5 | 2 | 561 | |
| 4P | 6 | 25 | 22.0 | 3.1 | 21.6 | 24.6 | 46.2 | 5.7 | 11.5 | 17.2 | 0.1 | 4.5 | 4.6 | 4 | 842 | |
| 5P | 7 | 25 | 30.1 | 9.0 | 7.8 | 7.5 | 15.3 | 12.9 | 12.8 | 25.7 | 2.4 | 14.0 | 3.5 | 5 | 744 | |
| X | 9 | 25 | 30.0 | 6.6 | 5.6 | 3.0 | 8.6 | 16.4 | 18.5 | 34.9 | 0.5 | 15.2 | 4.3 | 2 | 762 | |
| 2a | 11 | 25 | 8.6 | 1.6 | 14.2 | 28.9 | 43.1 | 13.5 | 26.5 | 40.0 | 3.0 | 3.0 | 0.6 | 12 | 931 | |
| 2a | 11 | 250 | 8.4 | 0.9 | 19.4 | 19.8 | 39.2 | 12.6 | 35.0 | 47.6 | 2.2 | 0.5 | 1.2 | 11 | 651 | |
| 3a | 12 | 25 | 9.5 | 1.8 | 24.1 | 22.5 | 46.6 | 14.0 | 23.4 | 37.4 | - | 3.7 | 1.0 | 16 | 779 | |
| D ₁₋₁₂ ^{pep} | 16 | 25 | 41.0 | 4.5 | 7.0 | 7.6 | 14.6 | 9.6 | 20.2 | 29.8 | 3.4 | - | 6.8 | 7 | 471 | |
| D ₁₋₁₆ ^{pep} | 16 | 250 | 26.6 | 4.8 | 11.9 | 19.4 | 31.3 | 4.2 | 13.1 | 17.3 | 12.3 | 2.4 | 4.5 | 6 | 620 | |
| E ₁₋₁₇ ^{pep} | 17 | 100 | 15.4 | 5.1 | 12.9 | 14.5 | 27.4 | 20.5 | 23.6 | 44.1 | 4.5 | 1.4 | 2.2 | 7 | 552 | |
| E ₁₋₁₇ ^{pep} | 17 | 1250 | 7.0 | 2.1 | 12.7 | 19.2 | 31.9 | 15.2 | 36.2 | 51.4 | 3.2 | 0.7 | 3.8 | 11 | 759 | |
| F ₁₋₁₈ ^{pep} | 18 | 25 | 17.8 | 4.8 | 14.5 | 19.3 | 33.8 | 8.6 | 24.3 | 32.9 | 7.2 | - | 3.4 | 9 | 580 | |
| F ₁₋₁₈ ^{pep} | 18 | 250 | 9.9 | 6.1 | 18.3 | 19.5 | 37.8 | 15.0 | 27.9 | 42.9 | 2.2 | 0.5 | 0.6 | 13 | 791 | |
| G ₁₋₁₉ ^{pep} | 19 | 25 | 19.9 | 9.7 | 14.4 | 17.0 | 31.4 | 8.8 | 15.3 | 24.1 | 9.7 | - | 5.2 | 5 | 659 | |
| H ₁₋₂₀ ^{pep} | 20 | 25 | 12.8 | 3.3 | 17.0 | 31.2 | 48.2 | 15.4 | 17.6 | 33.0 | 1.8 | 0.6 | 0.4 | 11 | 826 | |
| I ₁₋₂₁ ^{pep} | 21 | 25 | 19.2 | 9.0 | 11.9 | 30.0 | 41.9 | 7.9 | 20.9 | 28.8 | 1.4 | - | - | 8 | 708 | |
| J ₁₋₂₂ ^{pep} | 22 | 25 | 15.0 | 4.5 | 13.2 | 14.0 | 27.2 | 18.9 | 28.4 | 47.3 | 4.0 | 0.2 | 1.8 | 15 | 952 | |
| K ₁₋₂₃ ^{pep} | 23 | 25 | 28.6 | 14.9 | 3.9 | 6.5 | 10.4 | 3.2 | - | 3.2 | 6.5 | 14.3 | 22.1 | 1 | 154 | |
| L | 24 | 25 | 10.4 | 3.6 | 18.9 | 36.8 | 55.7 | 10.3 | 12.2 | 22.5 | 4.6 | 2.2 | 0.9 | 14 | 768 | |
| N | 26 | 100 | 13.8 | 3.6 | 13.6 | 16.4 | 30.0 | 12.4 | 14.2 | 26.6 | 1.5 | 19.8 | 4.6 | 14 | 675 | |
| control (without synthetic peptides) | | | 17.4 | 1.6 | 12.4 | 10.6 | 23.0 | 13.1 | 44.0 | 57.1 | 0.3 | 0.1 | 0.2 | 10 | 686 | |

Figure 8 – PEPTIDES DERIVED FROM NATURAL CASEIN STIMULATE LEUKOCTYE PROLIFERATION IN IRRADIATED, BONE MARROW RECONSTITUTED BALB MICE.

| Day After Treatment | 2 | | 4 | | 6 | | 9 | | 12 | | 15 | |
|---------------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| | Control | Chay-13 |
| 1 | 6 | 9 | 6 | 32 | 55 | 55 | 90 | 205 | 100 | 280 | 500 | 800 |
| 2 | 10 | 10 | 18 | 34 | 40 | 45 | 135 | 100 | 160 | 280 | 440 | 540 |
| 3 | 4 | 6 | 14 | 40 | 20 | 85 | 100 | 130 | 140 | 220 | 380 | 800 |
| 4 | 6 | 6 | 8 | 14 | 35 | 58 | 130 | 125 | 280 | 440 | 600 | 640 |
| 5 | 12 | 6 | 16 | 18 | 75 | 60 | 70 | 155 | 40 | 340 | 520 | 600 |
| 6 | 8 | 10 | 18 | 90 | 25 | 45 | 85 | 90 | 320 | 160 | 380 | 640 |
| Mean | 7.67 | 7.83 | 13.33 | 38* | 41.67 | 58* | 101.67 | 134.17 | 173.33 | 286.67 | 470 | 670 |
| SD | 2.69 | 1.86 | 4.71 | 24.95 | 18.63 | 13.42 | 23.57 | 38.01 | 97.75 | 88.44 | 78.95 | 97.81 |

* p < 0.008

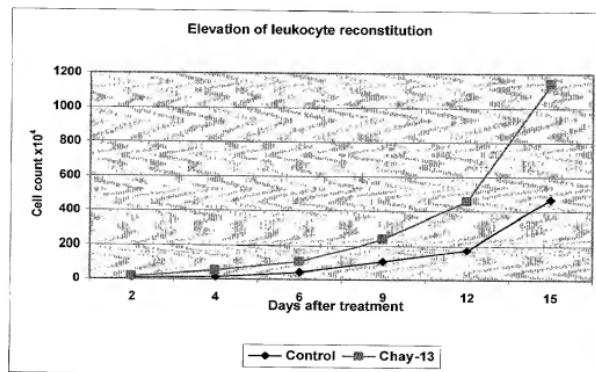


Figure 9 - PEPTIDES DERIVED FROM NATURAL CASEIN STIMULATE THROMBOCYTE PROLIFERATION IN IRRADIATED, BONE MARROW RECONSTITUTED BALB MICE.

| Days After treatment | 11 | | 13 | | 15 | |
|----------------------------|--------------|-------------|--------------|---------------|--------------|----------------|
| | Control | Chay-13 | Control | Chay-13 | Control | Chay-13 |
| 1 | 43 | 50 | 75 | 103 | 98 | 110 |
| 2 | 48 | 54 | 71 | 105 | 99 | 128 |
| 3 | 68 | 68 | 80 | 110 | 102 | 111 |
| 4 | 64 | 64 | 104 | 104 | 96 | 103 |
| 5 | 67 | 67 | 91 | 101 | 104 | 133 |
| 6 | 63 | 54 | 90 | 90 | 97 | 114 |
| 7 | 54 | 45 | 104 | 107 | 87 | 104 |
| 8 | | 63 | | 104 | | 116 |
| 9 | | 61 | | 93 | | 115 |
| 10 | | 57 | | 116 | | 112 |
| <i>Mean</i> | 58.14 | 58.3 | 87.86 | 103.3* | 97.57 | 114.6** |

* p < 0.01 ** p < 0.0001

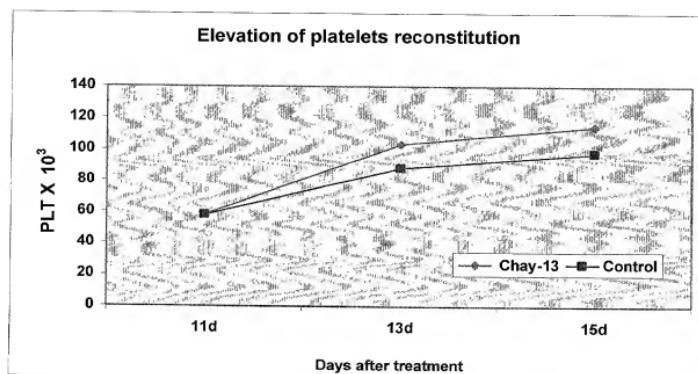
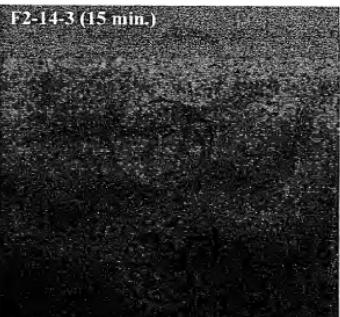
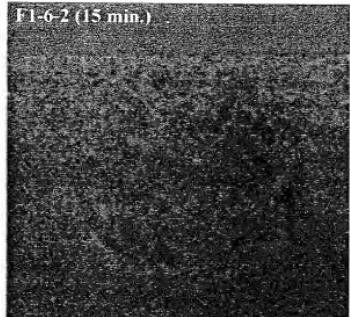


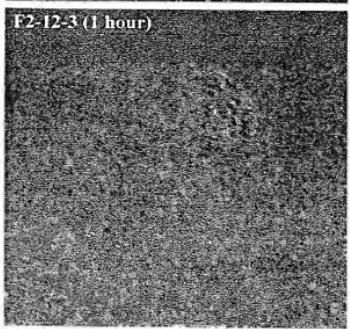
Fig. 9a



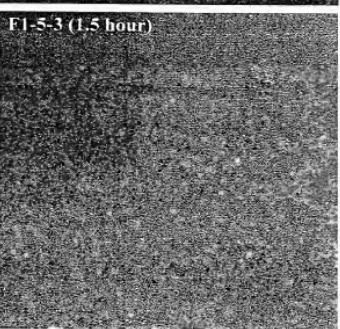
b



d



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FIG. 11 –Stimulation of Sup-T₁ Lymphocyte cell proliferation by Peptides Derived from Natural Casein.

| Chay13 ? g/ml | 3 days | | 7 days | |
|------------------|---------------|------------------------|---------------|------------------------|
| | cpm Counts | Proliferation Index | cpm Counts | Proliferation Index |
| 50 | 9268 | 1.18 | 120954 | 1.10 |
| 100 | 9940 | 1.26 | 112436 | 1.02 |
| 300 | 8425 | 1.07 | 102957 | 0.93 |
| 600 | 9771 | 1.24 | 101987 | 0.93 |
| 1000 | 8390 | 1.06 | 86649 | 0.79 |
| Control | 7802 | | 109560 | |

| Chay13 ? g/ml | 10 days | | 14 days | |
|------------------|---------------|------------------------|---------------|------------------------|
| | cpm Counts | Proliferation Index | cpm Counts | Proliferation Index |
| 50 | 17695 | 1.03 | 22272 | 1.36 |
| 100 | 19168 | 1.12 | 22842 | 1.40 |
| 300 | 21806 | 1.28 | 15318 | 0.93 |
| 600 | 22826 | 1.34 | 17368 | 1.06 |
| 1000 | 21764 | 1.28 | 10034 | 0.61 |
| Control | 17046 | | 16313 | |

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FIG.12 – Peptides Derived from Natural Casein inhibit of HIV-1 infection of CEM cells: Cell proliferation vs. P²⁴ Antigen levels.

| | Chay13 Ag/ml | CEM cells | |
|---------|-----------------|--|-----------------------------|
| | | Cell No. (x 10 ⁶) 15 days | P ²⁴ Ag Ng/ml |
| 3H | 50 | 0.29 | 16.39 |
| | 100 | 0.55 | 7.73 |
| | 300 | 0.54 | 1.61 |
| | 600 | 0.75 | 0.18 |
| | 1000 | 0.57 | 0.19 |
| 24H | 50 | 0.40 | 0.24 |
| | 100 | 0.48 | 4.21 |
| | 300 | 0.56 | 2.94 |
| | 600 | 0.62 | 0.18 |
| | 1000 | 0.79 | 4.03 |
| 48H | 50 | 0.37 | 10.05 |
| | 100 | 0.50 | 9.16 |
| | 300 | 0.56 | 3.21 |
| | 600 | 0.70 | 16.49 |
| | 1000 | 0.84 | 2.16 |
| Control | IF | 0.35 | 11.42 |
| | UIF | 0.42 | 0.17 |

FIG.13 – Synthetic Casein-Derived Peptides inhibit HIV-1 infection of CEM cells: Cell proliferation vs. P²⁴ Antigen levels.

| Peptide (3 hr pre-treatment) | Conc. μg/ml | CEM cells | |
|---------------------------------|----------------|--|-----------------------------|
| | | Cell No. (x 10 ⁶) 15 days | P ²⁴ Ag ng/ml |
| 1P (SEQ ID NO 3) | 100 | 1.29 | 0.17 |
| | 500 | 2.01 | 0.14 |
| 3P (SEQ ID NO 5) | 10 | 1.17 | 0.26 |
| | 25 | 1.26 | 0.18 |
| 4P (SEQ ID NO 6) | 25 | 1.26 | 0.42 |
| | 100 | 1.00 | 1.4 |
| | 250 | 1.59 | 0.10 |
| Control | IF | 1.06 | 0.52 |
| | UIF | 0.42 | 0.17 |

Fig. 14: Peptides Derived from Natural Casein Prevent Onset of Type I Diabetes in Non-Obese Diabetic mice.

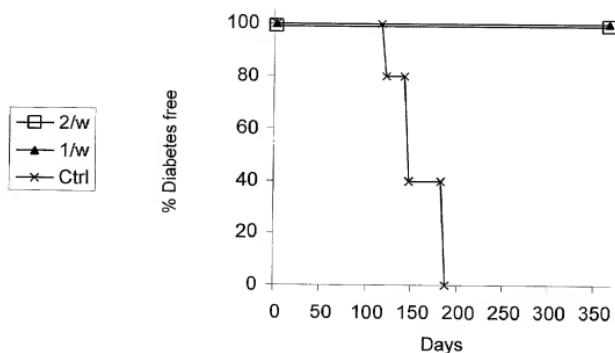


FIG. 15 - Total Cholesterol (TC), LDL & HDL levels in Hypercholesterolemic/Hyperlipidemic C57 black mice 1

| Sample* | Group** | Food | TC | HDL | LDL |
|---------|---------|----------|-----|-----|-----|
| 1 | Normal | Normal | 91 | 44 | <1 |
| | | Normal | 92 | 51 | <1 |
| 2 | | Enriched | 375 | 53 | 58 |
| | | Enriched | 411 | 46 | 51 |
| 3 | Control | Enriched | 411 | 46 | 51 |
| | | Enriched | 411 | 46 | 51 |
| 4 | | Enriched | 411 | 46 | 51 |
| | | Enriched | 411 | 46 | 51 |
| 5 | B | Enriched | 442 | 47 | 52 |
| | | Enriched | 445 | 38 | 42 |
| 6 | | Enriched | 409 | 47 | 52 |
| | | Enriched | 409 | 47 | 52 |
| 7 | C | Enriched | 411 | 34 | 37 |
| | | Enriched | 411 | 34 | 37 |
| 8 | | Enriched | 279 | 33 | 36 |
| | | Enriched | 278 | 43 | 47 |
| 9 | 2a | Enriched | 279 | 33 | 36 |
| | | Enriched | 278 | 43 | 47 |
| 10 | | Enriched | 312 | 38 | 42 |
| | | Enriched | 305 | 39 | 43 |
| 11 | 3P | Enriched | 312 | 38 | 42 |
| | | Enriched | 305 | 39 | 43 |
| 12 | | Enriched | 305 | 39 | 43 |

* One blood sample represents blood drawn from 2 mice

** Each group included 4 mice.

4

MEAN VALUES

| | | TC | HDL | LDL |
|-------|---------|-------|-------|-------|
| 1+2 | Normal | 91.5 | 49.75 | <1 |
| 3+4 | Control | 393 | 52 | 326.5 |
| 5+6 | B | 443.5 | 44.75 | 379 |
| 7+8 | C | 410 | 42.5 | 351 |
| 9+10 | 2a | 278.5 | 40 | 221 |
| 11+12 | 3P | 308.5 | 40.5 | 247 |

Cholesterol, HDL & LDL in C57 Black Mice Treated with Peptides

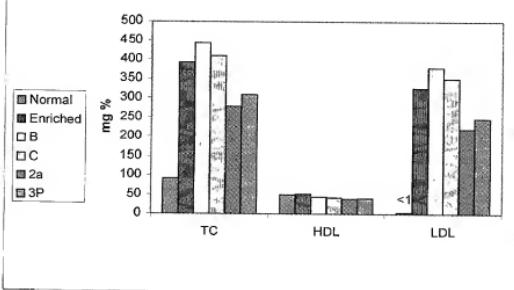


FIG. 16 - Effect of peptides derived from natural casein on cancer patients hematopoiesis.

| Patient | WBC | | PLT | | RBC | | HGB |
|---------|------------|---------------|--------------|-----------------|-----------|--------------|-----------|
| | Before | After | Before | After | Before | After | |
| 1 | 1,200 n | 4,100 241 | 17,000 n | 224,000 1217 | 3.27 n | 4.05 23 | 10.4 n |
| 2 | 5,400 n | 6,300 16.6 | 204,000 n | 259,000 26.9 | 3.37 n | 3.46 2.6 | 12.6 n |
| 3 | 3,400 n | 5,100 50 | 12,700 n | 17,900 40 | 4.49 n | 4.71 8.4 | 11.0 n |
| 4 | 700 n | 4,600 557 | 47,000 n | 151,000 221 | 2.88 n | 3.45 19.7 | 1.8 n |
| 5 | 4,900 n | 6,400 30 | | | | | |

WBC - White blood cells
PLT - Platelets
RBC - Red blood cells
HGB - Hemoglobin

Figure 17: Peptides Derived from Native Casein Stimulate Thrombocytopoiesis in Acute Myeloid Leukemia (Patient M-1).

| X | Y |
|-------|-------|
| 0 | 11 |
| 1 | 10 |
| 3 | 10 |
| 5 | 32.5 |
| 7 | 15 |
| 8 | 27.5 |
| 12 | 40 |
| 14.25 | 28 |
| 17 | 35 |
| 21 | 45 |
| 26.35 | 70.3 |
| 31.7 | 74 |
| 40 | 100.7 |

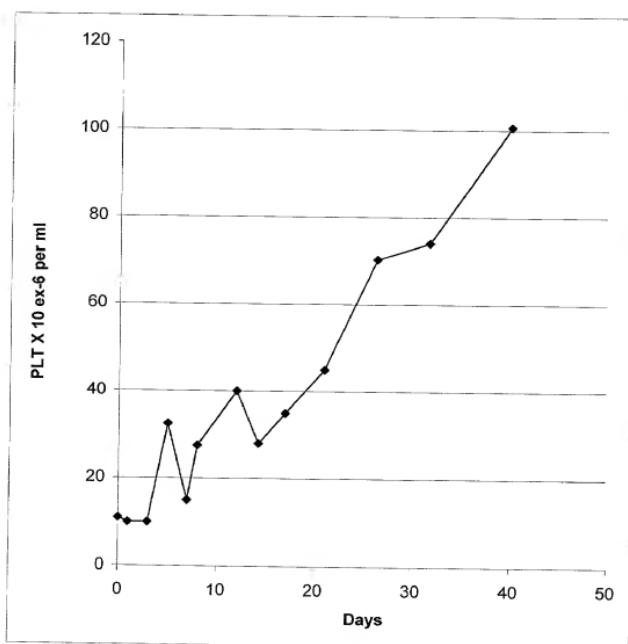


Figure 18: Peptides Derived From Native Casein Stimulate Thrombocytopoiesis in Acute Myeloid Leukemia (Patient M-2).

